REMARKS

Claims 1-11 remain in this application.

The present invention therefore provides a system allowing detection and/or efficient purification of biomolecules and/or proteins expressed at low level, preferably in their natural hosts, while maintaining them in functional complexes. It was not known previously that a combination of two affinity tags could be used for this purpose. The combination of tags required for this new application was not known and previously publications did not reveal that the combination disclosed would be successful.

Paragraph 5 and 6: Rejection under 35 USC 112, First Paragraph

In order to satisfy the enablement requirement of 35 U.S.C §112, first paragraph, the specification must teach one of skill in the art to make and use the invention. That some experimentation is needed, does not preclude enablement as long such experimentation is not undue. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. The claims includes the following elements.

a) providing an expression environment containing one or more heterologous nucleic acids encoding one or more subunits of a biomolecule complex;

One of ordinary skill in the art would clearly understand how to provide an expression environment. Numerous expression vectors are described in the literature and are commercially available. Depending on the biomolecule of interest, one of ordinary skill could easily purchase or routinely develop an expression vector for a given biomolecule. For example, the heterologous nucleic acid to be used is determined by the protein complex to be produced. Starting out from a certain biomolecule complex to be detected or purified, a skilled person can easily determine or identify the corresponding nucleic acid. Hence, providing such an expression environment would be nothing more than following well know directions well within the ordinary skill in this art.

(b) maintaining the expression environment under conditions that facilitate expression of the one or more subunits in a native form as fusion proteins with subunits being fused to at least two different affinity tags, wherein one of the affinity tags consists of one or more IgG binding domains of Staphylococcus protein A;

As vectors are described in the literature, so are conditions for their expression. It is well know that vectors can be provided that express biomolecules and/or proteins and that those proteins can be expressed a fused complex. Again, the expression is routine to one of ordinary skill.

(c) purifying the complex by a combination of at least two different affinity purification steps each comprising binding the two or more subunits via one affinity tag to a support material capable of selectively binding one of the affinity tags and separating the complex from the support material after substances not bound to the support material have been removed to provide a purified biomolecule and/or protein complex;

Purifying techniques, especially columns based purifying techniques are well known. Further, the example set forth in the specification illustrates a purification method.

(d) detecting the purified biomoleucle and/or protein complex

Methods of detection making use of affinity tags are well known. One of ordinary skill could easily determine how to detect a biomolecule of interest.

In addition, the following documents illustrate that the methods of the invention have been carried out in non-yeast cells.

Bouwmeester et al., Nat. Cell Biol. 2004 Feb.6(2): 97-105 (especially methods section);
WO 04/035783;
WO 04/031242;
WO 04/009622;
WO 04/009619;
WO 04/007544.

From these numerous documents, it is clear that the cells and conditions, respectively, used in the Examples of the present application are merely one specific embodiment of a plurality of other possibilities and that one of ordinary skill was easily able to make the methods work with other cells and with other conditions.

Paragraph 8: Rejection under 35 USC 112, Second Paragraph

Claim 1 has been amended to clarify that a fusion protein is expressed.

Paragraph 9

The term "other components" has been deleted.

Paragraph 10 and 11

The claims have been amended to recite all steps in the process.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

The Commissioner is hereby authorized to charge any additional fees which may be required in this application to Deposit Account No. 06-1135.

Respectfully submitted,
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